

**Specification.**

On page 1, please replace the title with the following:

**-- A MICROELECTRONIC DEVICE FOR ELECTROCHEMICAL  
DETECTION OF NUCLEIC ACID HYBRIDIZATION --**

Please replace the paragraph on page 1, lines 1–4 with the following:

**-- Cross-Reference to Related Applications**

This application is a divisional application of application Serial No. 09/603,217 filed June 26, 2000, now U.S. Patent No. 6,361,951, which is a divisional application of application Serial No. 09/179,665 filed October 27, 1998, now U.S. Patent No. 6,132,971, which is a divisional application of application Serial No. 08/667,338 filed June 20, 1996, now U.S. Patent No. 5,871,918, which is a continuation-in-part of application Serial No. 60/016,265 filed April 19, 1996, which is a continuation-in-part of copending application Serial No. 08/495,817 filed June 27, 1995, ~~abandoned, and is a continuation-in-part of copending provisional application Serial No. 60/016,265 filed April 19, 1996,~~ which claims benefit of provisional application Serial No. 60/060,949 filed June 27, 1995, the disclosures of which are incorporated by reference herein in their entirety. --

Please replace the paragraph on page 5, lines 1–9 with the following:

-- **Figure 2** shows the cyclic voltammograms of  $\text{Ru}(\text{bpy})_3^{2+}$  in the presence of 5'-AAATATAGTATAAAA (**SEQ ID NO: 1**) as a single strand (C) and hybridized to complementary strands (A & B). The scan rate is 25 mV/s. (A) represents 25  $\mu\text{M}$   $\text{Ru}(\text{bpy})_3^{2+}$  + 100  $\mu\text{M}$  (in guanine nucleotides) double stranded fully hybridized DNA (5'-AAATATAGTATAAAA, **SEQ ID NO: 1**)•(3'-TTTATATCATATTTT, **SEQ ID NO: 2**). (B) represents  $\text{Ru}(\text{bpy})_3^{2+}$  with a duplex containing a GA mismatch (5'-AAATATAGTATAAAA, **SEQ ID NO: 1**)•(3'-TTTATATAATATTTT, **SEQ ID NO: 3**), and (C) represents  $\text{Ru}(\text{bpy})_3^{2+}$  a single strand containing one guanine nucleotide (5'-AAATATAGTATAAAA, **SEQ ID NO: 1**). -

Please replace the paragraph on page 5, lines 15–21 with the following:

**Figure 5** shows the cyclic voltammograms of  $\text{Ru}(\text{bpy})_3^{2+}$  (25  $\mu\text{M}$ ) at a scan rate of 25 mV/s in 50 mM sodium phosphate buffer with 0.7 M NaCl, pH 7. (A) No added oligonucleotide. (B) With 75  $\mu\text{M}$  d[5'-TTTTATACTATATTT, SEQ ID NO: 2]. (C) With 75  $\mu\text{M}$  of the hybrid of the oligomer from B and d[5'-GGGAAATATAGTATAAAAGGG, SEQ ID NO: 4]. Working electrode: tin-doped indium oxide. Reference electrode: Ag/AgCl. Counter electrode: Pt wire. The secondary structure of the hybrid from C is indicated on the Figure.

Please replace the paragraphs on page 6, lines 17–26 with the following:

**Figure 14** shows the cyclic voltammogram of  $\text{Ru}(\text{bpy})_3^{2+}$  (25  $\mu\text{M}$ ) alone and with (100  $\mu\text{M}$  in strands) of 5'-AAATATAG<sub>n</sub>TATAAAA (SEQ ID NO: 5) where n = 1 (G), 2 (GG), or 3 (GGG). The scan rate is 25 mV/s.

**Figure 15** shows the cyclic voltammogram of  $\text{Ru}(\text{bpy})_3^{2+}$  (25  $\mu\text{M}$ ) alone and with (100  $\mu\text{M}$  in strands) of 5'-AAATAT(AGT)<sub>n</sub>ATAAAA (SEQ ID NO: 6) where n = 1, 2, or 3. The scan rate is 25 mV/s.

**Figure 16** shows the cyclic voltammogram of 25  $\mu\text{M}$  Ruthenium (4,4'-dimethylbipyridine)<sub>3</sub><sup>2+</sup> (or " $\text{Ru}(4,4'\text{-Me}_2\text{-bpy})_3^{2+}$ ") alone (solid) and with (100  $\mu\text{M}$  in strands) of 5'-AAATATAGTATAAAA (SEQ ID NO: 1, dotted) and 5'-AAATATAGGGTATAAAA (SEQ ID NO: 5, dashed). The scan rate is 25 mV/s.

Please replace Table 1 starting on page 37, line 18 with the following:

**Table 1. Rate Constants for Oxidation of Guanine in DNA Oligomers by Ru(bpy)<sub>3</sub><sup>2+</sup>**

$k(\text{M}^{-1} \text{s}^{-1})^a$	oligomer sequence	$\Delta r_{\text{Ru-G}}(\text{\AA})^b$
$1.2 \times 10^3$	(5' -AAATATAGTATAAAA, <u>SEQ ID NO: 1</u> ) • (3' -TTTATATCATATTTT, <u>SEQ ID NO: 2</u> ) GC pair	1.7 Å
$5.1 \times 10^3$	(5' -AAATATAGTATAAAA, <u>SEQ ID NO: 1</u> ) • (3' -TTTATATTATATTTT, <u>SEQ ID NO: 7</u> ) GT mismatch	1.2 Å
$1.0 \times 10^{4c}$	(5' -AAATATAGTATAAAA, <u>SEQ ID NO: 1</u> ) • (3' -TTTATATGATATTTT, <u>SEQ ID NO: 8</u> ) GG mismatch	1.0 Å
$1.9 \times 10^4$	(5' -AAATATAGTATAAAA, <u>SEQ ID NO: 1</u> ) • (3' -TTTATATAATATTTT, <u>SEQ ID NO: 3</u> ) GA mismatch	0.7 Å
$1.8 \times 10^5$	(5' -AAATATAGTATAAAA, <u>SEQ ID NO: 1</u> ) single strand	0 Å
$5.1 \times 10^3$	(5' -AAATATAGTATAAAA, <u>SEQ ID NO: 1</u> ) • (3' -TTTATATCTATTTT, <u>SEQ ID NO: 9</u> )	1.2 Å

<sup>a</sup>DNA concentrations used to determine rate constants were based on the moles of guanine nucleotides.

<sup>b</sup>Estimated distance of tunneling through solvent. Distances calculated according to  $k/k_{ss} = \exp[-\beta\Delta r]$ , where  $\beta(\text{H}_2\text{O}) = 3 \text{\AA}^{-1}$  and  $k_{ss} = 1.8 \times 10^5 \text{M}^{-1}\text{s}^{-1}$ . <sup>c</sup>Since the rate constants are relative to guanine concentrations, the observed rate for the GG mismatch has been normalized relative to the other oligomers containing a single guanine.

Please enter the attached paper copy of the Sequence Listing at the end of the specification.

Attachment: paper copy of Sequence Listing